REMARKS

Claims 19-38 currently appear in this application. The Office Action of May 20, 2003, has been carefully studied. Claims 19-33 are allowed. It is believed that all of claims 19-38 define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Claims 34-36 are rejected under 35 U.S.C. 112, first paragraph because the specification is said not to be enabling for any pH- or potential sensitive fluorophore without other structural information which reacts with any surface whatsoever.

This rejection is respectfully traversed. Submitted herewith are PowerPoint slides showing results obtained using two polymers: dextran-spermine and arabinogalactan-spermine.

Slide 1 is a general structure of a sugar-based polycation as used in the examples described hereinafter.

Slide 2 is a chemical scheme for the synthesis procedure for obtaining sugar-based polyglycan.

Slide 3 provides the chemical composition of polysaccahride-spermine conjugates.

Slide 4 shows the chemical characterization of the sugar-based polycation conjugates described herein.

Slide 5 shows the elctrostatics of spermine conjugates determined through covalently attached hydroxycoumarin.

Slide 6 shows the electrostatics of polysaccharide spermine conjugates.

Slide 7 shows electrostatics neutralization of polymers covalently attached to a probe. This slide makes it very clear that the potential of the polymer surface is altered when DNA binds to the surface thereof.

Slide 8 shows that electrostatic neutralization of polymers covalently attached to a probe act in a dose dependent manner.

It can readily be seen from the above slides that with polymer-based surfaces, it is possible to determine the binding of species (in this case, DNA) to a polymer surface which is covalently liked with a probe.

The same experiments could have been conducted with other, commonly used probes, with the same expectation of success, taking into consideration the limitation that the probe is covalently linked to the polymer.

Claims 34 and 36 are very clearly written to claim only the use of a probe having a pH- or potential-sensitive

fluorophore with a species at a polymer surface which has a local environment at a given pH or surface potential. It is clear that the fluorophore is incorporated at the surface of a polymer, and the polymer must be one which has a pH or surface potential that can be measured.

Claim 36 is even more specific, in limiting the probe to a pH- or potential-surface fluorophore attached to a steroid, to a head group of a sphingolipid or to a head group of a lipid having at least two hydrophobic chains.

Claims 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 34 and 35 encompass a genus of fluorophores whose fluorescence depends on the binding or dissociation of a species at a surface. The surface is the surface of a polymer surface which has a local environment at a given pH or surface potential. That is, the fluorophores are those which detect binding by detecting change of pH or change of surface potential in the environment surrounding the fluorophore.

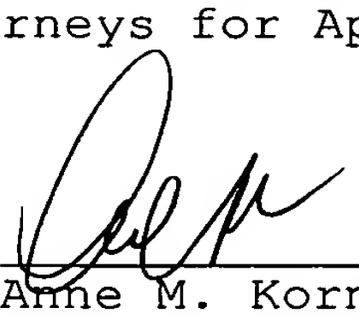
In rejecting the claims for lack of enablement, the Examiner has cited *The Regents of the University of California*

v. Eli Lilly and Co., 43 USPQ 2d 1398 (Fed. Cir. 1997); *Fiers v .Sugano*, 25 USPQ 2d1601 (Fed. Cir. 1993) and *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ 2d 1111 (Fed. Cir. 1991). The first two of these cases dealt with genes and DNA, respectively, in which the subject matter was described only by function. *Vas-Cath* dealt with using the drawings to satisfy the written description requirement. It is well appreciated that description of a gene or DNA by function is, at this time, still somewhat indefinite in defining the gene or DNA. However, it is respectfully submitted that one skilled in the art (*e.g.*, an analytical chemist who is conversant with the properties of fluorophores having different structures) can readily determine if a fluorophore binds to a species and changes fluorescent properties in response to a change in pH or potential. This determination can be effected without undue experimentation, as those skilled in the art can readily determine which fluorophores respond to changes in pH or potential, and which fluorophores could be covalently attached to a polymer surface.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant

By 
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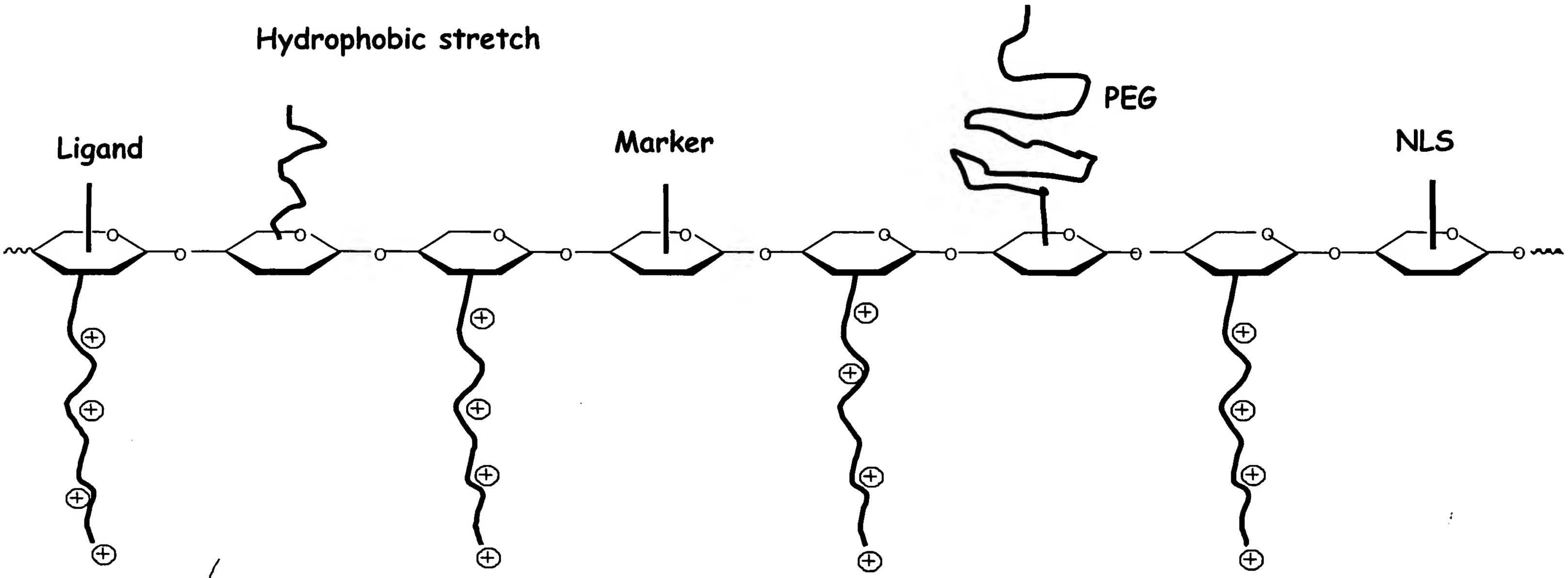
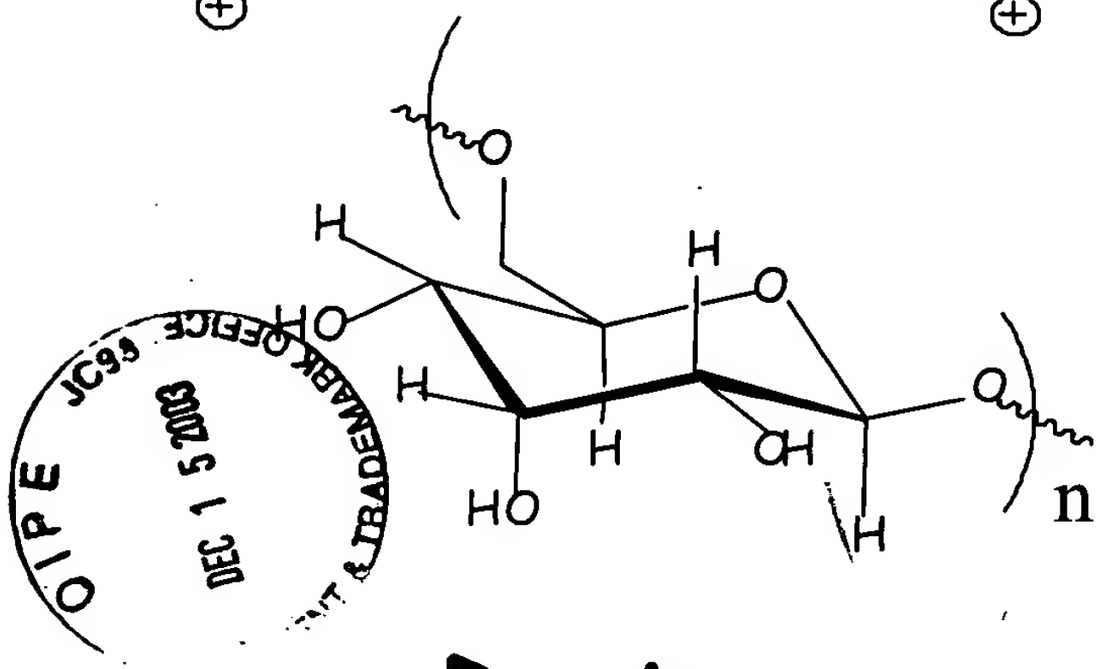
Our modular biodegradable polycation

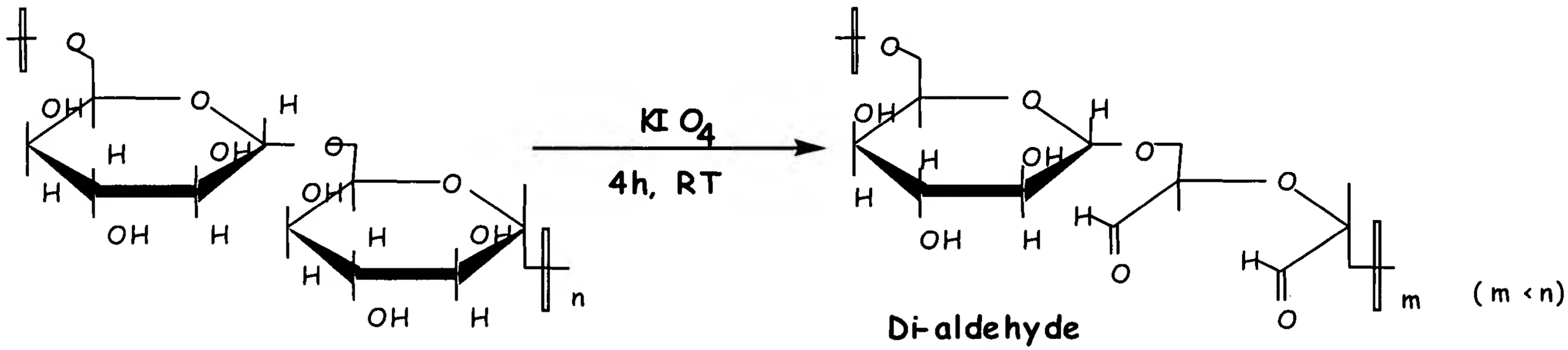




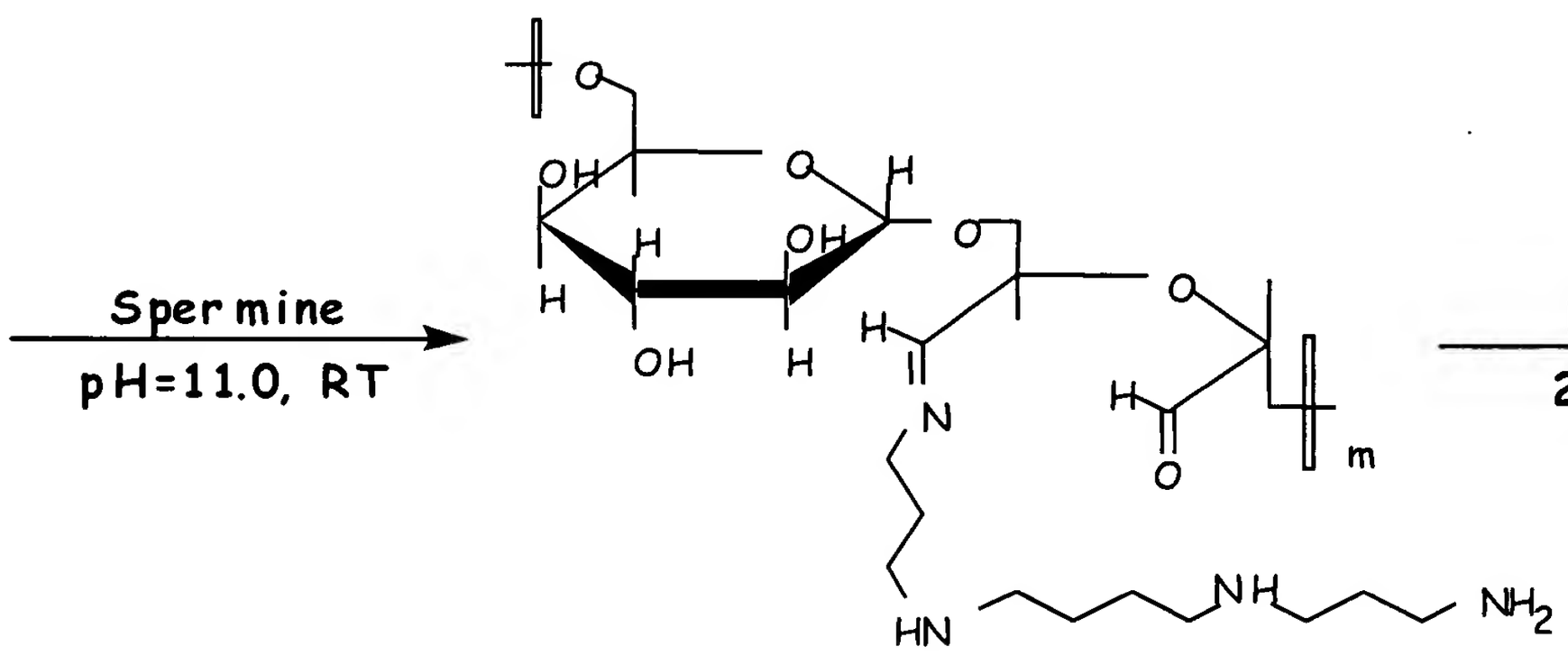
Dextran

- Biodegradable backbone
- Control of cationic density & distribution
- Multifunctional

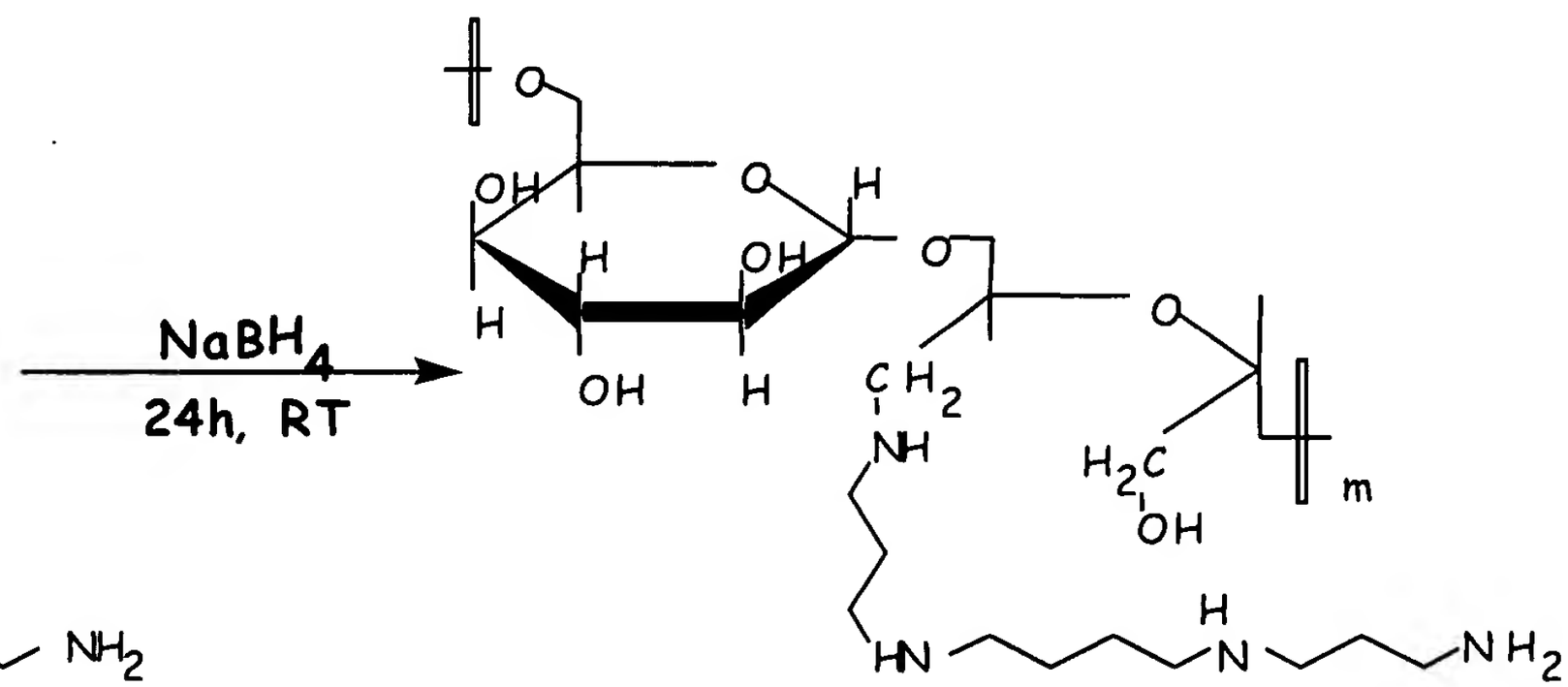
Novel cationic polysaccaride system



Di-aldehyde polysaccharide



Polysaccharide -Spermine (Imine conjugate)



Polysaccharide -Spermine (Amine conjugate)

Chemical composition of polysaccharide-spermine conjugates

Polymer code	chemical composition (Saccharide/KIO_4)
TA1-126A	Arabinogalactan(1:1)-Spermine
TA1-127A	Arabinogalactan(1:3)- Spermine
TA1-127B	Arabinogalactan(1:5)- Spermine
TA1-129A	**Dextran(1:1)- Spermine**
TA1-129B	Dextran(1:3)- Spermine

	DOTAP/Cholesterol (1:1)

Chemical characterization of conjugates

Polymer code	Composition	Nitrogen[a] (% weight)	Primary amino groups[b] (nmole/mg)	Spermine moieties[c] (nmole/mg)	Secondary amino groups[d] (nmole/mg)	Crosslinked spermine[e] (%)
TA1-126A	AG(1:1)-S	8.31	1600	1480	4400	0
TA1-127A	AG(1:3)-S	3.91	750	700	2100	0
TA1-127B	AG(1:5)-S	2.66	520	480	1440	0
TA1-129A	**DEX(1:1)-S**	**11.19**	**1100**	**2000**	**6000**	**45**
TA1-129B	DEX(1:3)-S	4.85	890	870	2610	0

(a) determined by elemental analysis

(b) determined by TNBS method

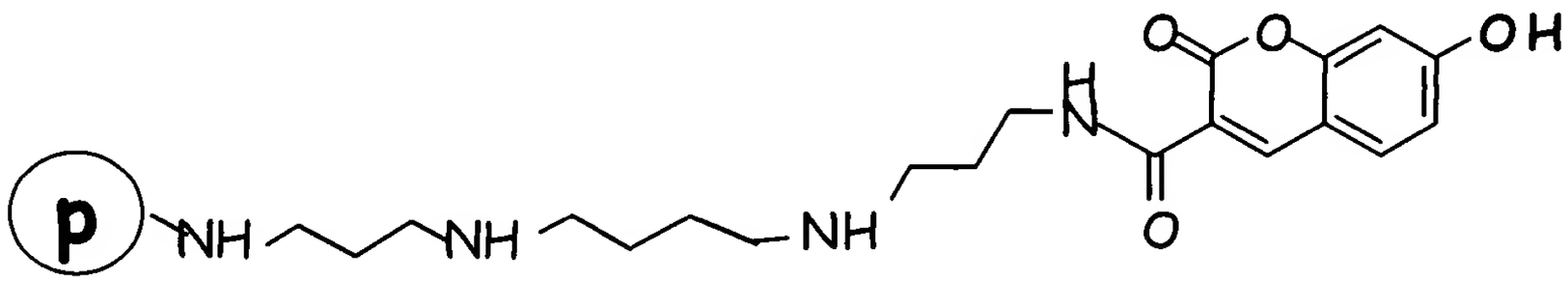
(c) calculated from elemental analysis (total Nitrogen divided by 4)

(d) calculated from spermine (spermine content multiply by 3)

(e) (Total Nitrogen - primary amino groups - secondary amino groups)*100/(spermine)

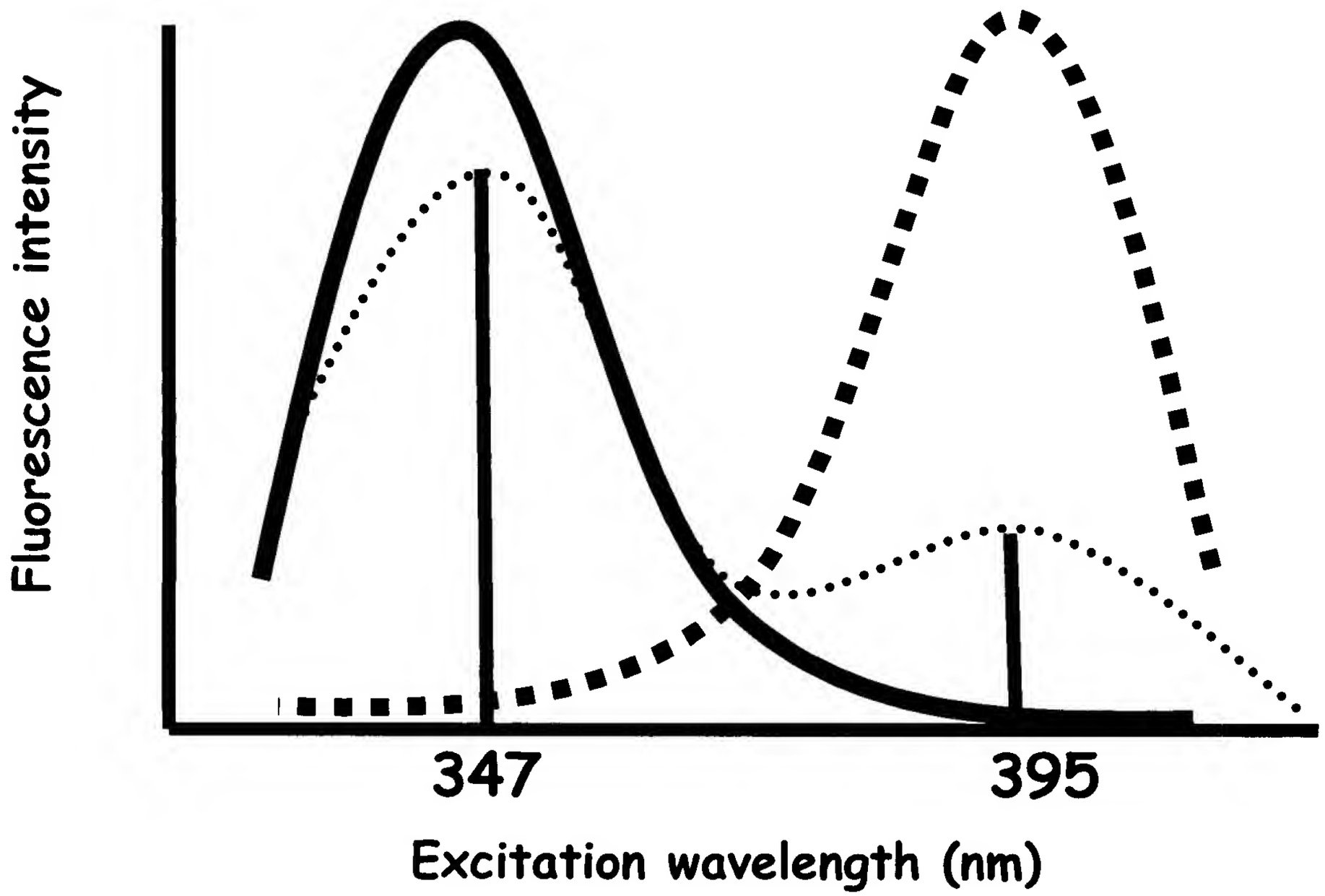
Abbreviations: AG-arabinogalactan; DEX-dextran; S-spermine.

Electrostatics of spermine conjugates determined trough covalently-attached hydroxycoumarin



pH<pKa$_{(HC)}$ protonated

pH>pKa$_{(HC)}$ unprotonated



Total probe = $I_{347}+I_{395}$

Dissociation degree (/) =

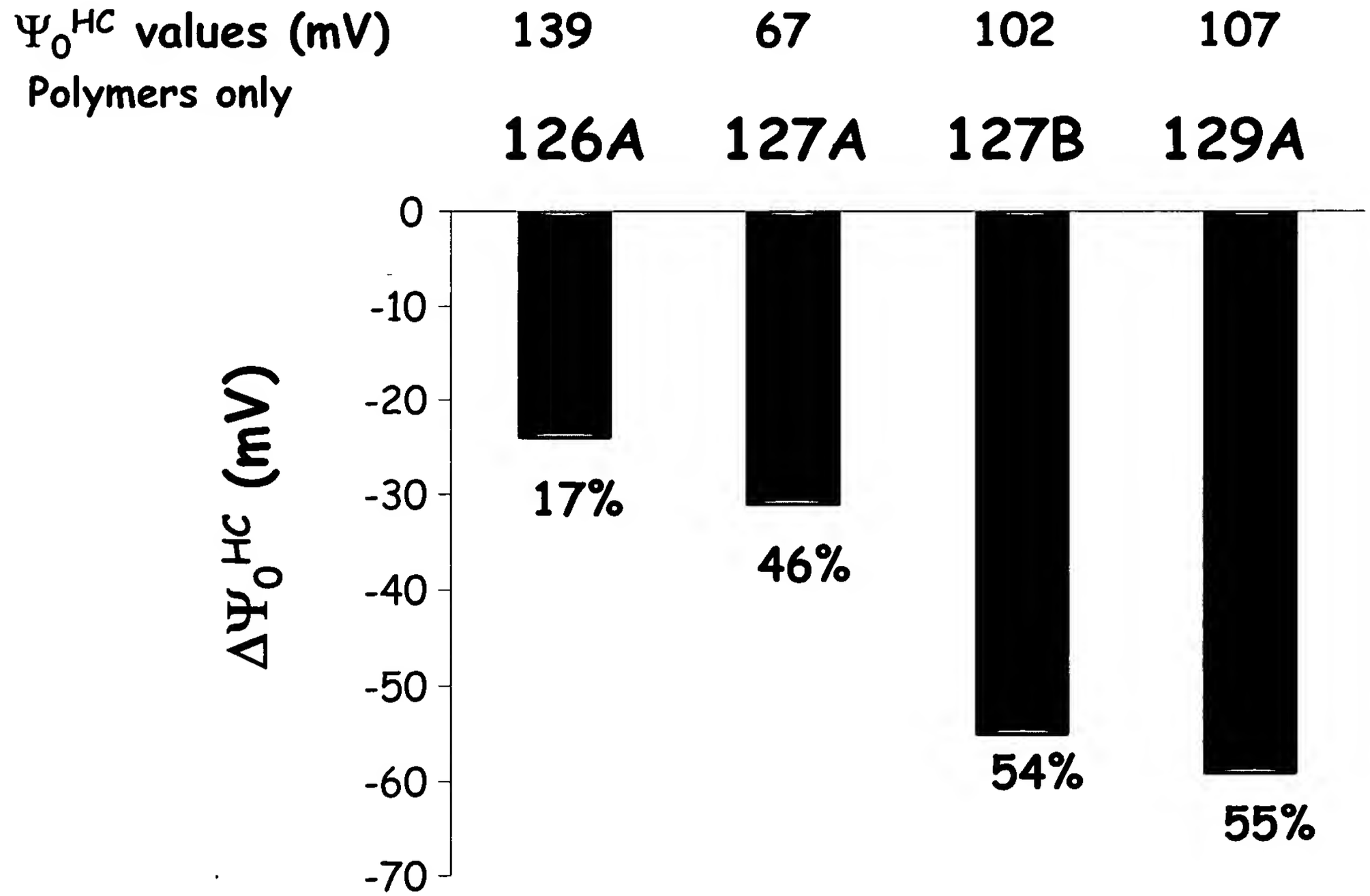
$I_{395}*100/(I_{347}+I_{395})$

<1% labeling

Electrostatics of polysaccharide spermine conjugates

polymer	Apparent pKa	Ψ_0 (mV)	$pH_{surface}$ 20 mM Hepes, pH 7.4
HC	7.8		
TA1-126A	5.4	139	9.8
TA1-127A	6.7	67	8.5
TA1-127B	6.0	102	9.2
TA1-129A	6.0	107	9.2
TA1-129B	6.7	64	8.5

Electrostatic neutralization of polymers by DNA



Decreased electric surface potential upon DNA addition (charge ratio of 2.0 DNA^-/NH_3^+)

Electrostatic neutralization of polymers by DNA